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ROLE OF CARBON DIOXIDE IN INERT GAS NARCOSIS.(U)
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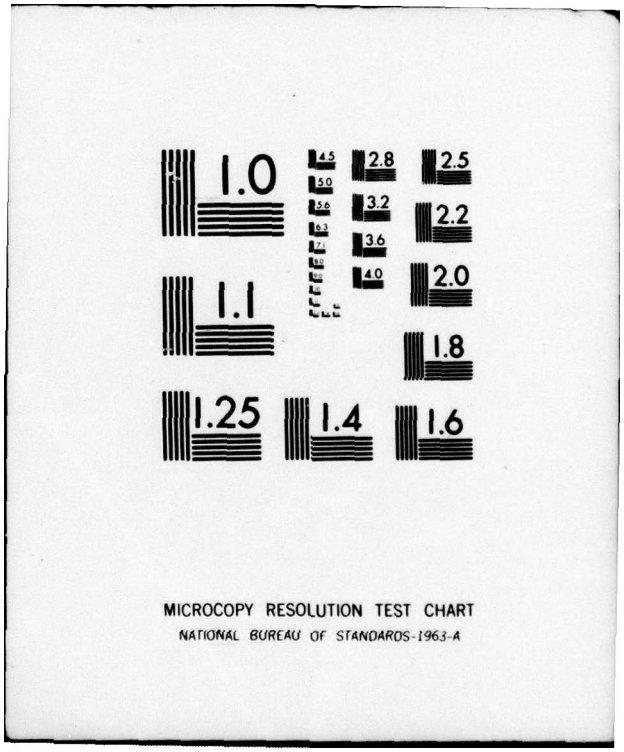
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# REPORT

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THE OHIO STATE UNIVERSITY
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1314 KINNEAR RD.
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To DEPARTMENT OF THE NAVY
Office of Naval Research
Arlington, Virginia 22217

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On ROLE OF CARBON DIOXIDE IN INERT GAS NARCOSIS

For the period May 1, 1974 - December 31, 1976

Submitted by Dr. Harold S. Weiss
Department of Physiology

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The role of carbon dioxide and oxygen in high pressure narcosis was studied by exposing animals to hyperbaric conditions while maintaining them normoxic and normocapnic. Chickens were the experimental animals used since the avian respiratory anatomy lends itself to a surgical modification that allows a unidirectional flow of gas through the pulmonary system and eliminates dead space. Heated, humidified gas entered the lung via a tracheal cannula and exited from the posterior air sacs via cannulae through the body wall. If the mass flow of gas through the lungs is much greater than the normal flow, then the bird's own respiratory (con't.)

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gas exchange will not significantly affect the composition of the gas. Therefore the lung $P_{CO_2}$ and $P_{O_2}$ and P(inert) can be maintained at any level chosen for the inflow gas. The unanaesthetized restrained birds were exposed to pressures up to 6 atmospheres absolute (ATA) in a hyperbaric chamber.

Narcosis was estimated from changes in the visually evoked response (VER). The VER was recorded from the optic tectum by means of implanted bipolar fine wire electrodes. The VER was initiated by an external strobe light. A depression of the amplitude of the VER is considered to reflect narcosis.

All animals showed a strong depression in VER amplitude on exposure to normoxic, normocapnic gas at 6 ATA when the inert component was nitrogen; the onset of the depression was a smooth function of depth. No depression of VER was seen when the inert diluent was helium. Increasing lung $P_{CO_2}$ to 70 mmHg had no effect on VER. Therefore depression of VER appears to be a reflection of narcosis induced by high nitrogen pressure and not solely hypoxia, hypercapnia or pressure per se. Relatively small changes in the body temperature (1.5 C) depressed VER and may explain some of the depression of VER seen by others with helium. Resistance to the high flow of gas through the bird was usually 7.5 - 10 cm $H_2O$ at a flow rate of 6 $\ell$/min ambient temperature and pressure; this resistance remains nearly constant over the 1 - 6 ATA pressure range investigated.

# The Role of Carbon Dioxide in Inert Gas Narcosis

Narcosis induced by breathing compressed air at elevated pressures has been known since the 1800s but the mechanism of action is still debated. The most widely held theory considers narcosis to be a direct effect of the increased quantity of nitrogen ($N_2$) dissolved in tissues under high pressure. The dissolved $N_2$ is believed to interfere with neural function by changing permeability and/or electrical polarization of cells and cellular membranes. This theory appears to fit in well with the Meyer-Overton view of anesthesia.

A competing hypothesis suggests that the neural disturbances are brought about by hypercapnia and hypoxia. It is presumed that hyperbaria increases gas density and viscosity to the point where respiratory flow is inhibited, leading to retention of carbon dioxide ($CO_2$) and a deficiency of oxygen ($O_2$). Acceptance of this theory appeared to be declining, in part because gases like xenon are narcotic at sea-level pressures and in part because $N_2$ narcosis was not alleviated in man when ventilation was assisted by pump. However, it has been restimulated by an analysis which suggests that rather than simple inhibition of flow, subsegmental bronchioles may collapse on expiration when gas of increased density flows through them at velocities associated with normal ventilatory rates. The collapsed passages would effectively reduce the diffusion area and lead to hypercapnia and hypoxia. This revised theory can also explain the xenon effects at sea-level pressure, and the failure of narcosis to be relieved by a respiratory pump in the circuit.

Experimentally, it has been difficult to substantiate or refute the hypoxia/hypercapnia concept, in part because of problems associated with measuring oxygen and carbon dioxide tensions ($P_{O_2}$, $P_{CO_2}$) in arterial blood while at elevated pressures. Our experimental approach was somewhat different; namely, to use the unique characteristics of the avian lung to establish any desired concentration of gases at the blood-gas exchange surface. This is possible in Aves because pulmonary gas flow can be made unidirectional through the interconnecting network of air capillaries and air sacs which replace the mammalian alveoli and diaphragm. Pulmonary $P_{CO_2}$, $P_{O_2}$, and $P_{N_2}$ can thus be controlled independently at any desired pressure and flow and with no dead space.

In this study the role of carbon dioxide and oxygen in high-pressure narcosis was examined by exposing unanesthetized, mildly restrained chickens to hyperbaric conditions while maintaining them normoxic and normocapnic. The chickens were surgically modified to allow the unidirectional flow of heated, humidified gas to enter the lung via a tracheal cannula and to exit from the posterior air sacs via cannulae through the body wall. The mass flow of gas through the lungs was 10 times the normal flow, effectively preventing the bird's own respiratory gas exchange from significantly altering the composition of the pulmonary gas. $P_{CO_2}$, $P_{O_2}$, and $P_{inert}$ in the lung was therefore maintained at the level chosen for the inflow gas.

The unanesthetized, restrained birds were exposed to pressures up to six atmospheres absolute (ATA) in a hyperbaric chamber. Narcosis was estimated from changes in the visually evoked response (VER). The VER was recorded from the optic tectum of the brain by means of implanted bipolar fine-wire electrodes. The VER was initiated by an external strobe light. A depression of the amplitude of the VER was considered to reflect narcosis.

All animals showed a strong depression in VER amplitude on exposure to normoxic, normocapnic gas at 6 ATA when the inert component was $N_2$; the onset of the depression was a smooth function of depth. No depression of VER was seen when the inert diluent was helium (He). In birds at 6 ATA with $N_2$, increasing lung $P_{O2}$ to the equivalent of 60% $O_2$ at sea level and decreasing lung $P_{CO2}$ below 4% sea-level equivalent did not bring about any recovery of the depressed VER. Therefore depression of VER appears to be a reflection of narcosis induced by high nitrogen pressure and not of hypoxia, hypercapnia, or pressure per se.

Minimal effects of $CO_2$ were confirmed when increasing lung $P_{CO2}$ to 70 mmHg or decreasing it to near zero mmHg had no demonstrable effect on the VER of the bird at sea level. The avian brain however, seems very sensitive to hypoxia, since decreasing lung $P_{O2}$ only to the 120-130 mmHg range depressed the VER. Relatively small changes in the body temperature (1.5°C) also depressed the VER. In view of the high heat conductivity of He, this may explain some of the reports of narcotic effects with helium. Resistance to the high flow of gas through the bird was usually 7.5 - 10 cm $H_2O$ at a flow rate of 6 $\ell$/min at ambient temperature and pressure; this resistance remains nearly constant over the 1-6 ATA pressure range investigated.

Lack of a satisfactory animal preparation appears to have inhibited experimental work on inert gas narcosis. The awake, unidirectionally ventilated chicken prepared for recording the VER appears to be an animal model well suited for such studies. It may serve to carry out comparisons among inert gases, on various combinations of $O_2$ (particularly hypoxia) and $CO_2$ with the inert gases, and also for evaluating a range of pharmacological and physical factors (e.g., temperature) believed important in narcosis.

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